Remarks

In this response, Applicants have cancelled Claims 31, 32, 38, 39, 45, and 46. Applicants have presented arguments to overcome the Examiner's rejections. The pending claims have not been amended, but are reproduced for the Examiner's convenience.

REJECTION UNDER 35 U.S.C. § 112 FIRST PARAGRAPH

Claims 27-33 stand rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that is not enabled. The Examiner stated the Specification is "enabling for shelf stable solution formulation comprising SEQ ID NO: 2 and GLP-1 analogs: 7-34; 7-35; 7-36; 7-37." However, the Examiner suggests that the Specification does not reasonably provide enablement for any *one* additional amino acid substitution at another position in the GLP-1 molecule.

The burden is on the Examiner to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright,* 999 F.2d 1557, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). See also MPEP § 2164.04. In examining a patent application, the PTO is required to assume that the specification complies with the enablement provision of § 112 unless it has acceptable evidence or reasoning to suggest otherwise. *In re Marzocchi,* 439 F.2d 220, 223, 169 USPQ 367, 369-370 (C.C.P.A. 1971).

> [I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.

Id. at 224. The reasons stated by the Examiner as to why the invention is not enabled are overcome by the skill of the artisan and the prior art.

In past office actions (Paper Nos. 8 and 11), the Examiner has raised obviousness rejections that the claimed subject matter is not patentable over the prior art. (See for example Paper No. 11, page 6, last paragraph; "Therefore, it would have been obvious to one of skill in the art to arrive at the claimed invention as a whole because the combined teaching of Andrews et al., Jensen et al. and Smith et al. results in the claimed invention of a shelf stable solution formulation comprising glucagon-like-peptide- 1 (GLP- 1), a pharmaceutically acceptable preservative, a tonicity modifier, and a process for preparation thereof for the treatment of diabetes.")

Now, in this office action, the Examiner has raised an enablement rejection. While not explicitly doing so, the Examiner appears to be selectively using the prior art to support

an obviousness rejection, while not considering it to be skill of the art when making an enablement rejection. Applicants respectfully submit that this is inappropriate. The Federal Circuit has commented negatively on the inconsistency of saying on the one hand that prior art in combination taught a skilled person how to make and use an invention, and on the other hand saying that this prior art plus Applicants' specification did not adequately enable a skilled person to make and use the invention. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 (Fed. Cir. 1986). In *Hybritech*, the court noting the inconsistency in the trial courts application of the law stated:

> Taken as a whole, the court's comments on § 112 . . . are internally inconsistent. . . . The district court itself stated that the "method for producing monoclonal antibodies in vitro was well known prior to the alleged invention". . . . The court then about-faced and held the '110 patent deficient because it fails to teach how to make monoclonal antibodies.

Id. at 1384. The Federal Circuit reversed the trial court and found the claims at issue to be valid.

Applicants have described and enabled a novel and nonobvious shelf stable solution formulation as evidenced in the examples. (See pp.15-16 of Applicants' specification). These data alone are sufficient to establish the enablement of the claimed invention. The specification expressly contemplates the use of not only natural GLP-1, but also analogs, derivatives and salts of GLP-1 in the shelf stable solution formulation. (See p. 8 of the Specification) The specification also states that a "GLP-1 analog is defined as a molecule having one or more amino acid substitutions, deletions, inversions, or additions relative to GLP-1(7-37)." (P. 9) The Specification also discloses known GLP-1 analogs as being consistent with the GLP-1 analogs of the invention. (See pp 9-12) Thus, the invention is directed to a shelf stable formulation that comprises *any* GLP-1 molecule, a pharmaceutically acceptable preservative; and a tonicity modifier, and wherein the formulation has a pH that is about 8.2 to about 8.8. Applicants' claims are limited to a GLP-1 molecule having a specific amino acid sequence (SEQ ID NO. 2) and further comprising one additional amino acid substitution. This genus of GLP-1 molecules represents a reasonable scope supported by sufficient evidence. Applicants respectfully request withdrawal of this rejection.

REJECTION UNDER 35 U.S.C. § 112 SECOND PARAGRAPH

Claims 27-33 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Applicants respectfully submit that the language "and further comprises one additional amino acid substitution" is clear. The additional amino acid substitution can be anywhere on the GLP-1 molecule that is not contemplated by the variables X, Y, Z, RI or R2.

Claim 28 stands rejected under 35 U.S.C. § 112, second paragraph as being indefinite with reference to the term "about." This rejection is inconsistent with the law and the practice of the Patent Office. The MPEP states that "about" is definite unless there is close prior art. (MPEP § 2173.05(b)(A)). (*See also Ex parte Eastwood,* 163 USPQ 303 (Bd. App. 1968) and *W.L. Gore v. Garlock, Inc.,* 721 F.2d 1540 (Fed. Cir. 1983)). Here there is no prior art that would render the term "about" indefinite. Applicants respectfully request reconsideration and withdrawal of this rejection. Applicants respectfully submit that the metes and bounds of the claim are clear and request the §112 second paragraph rejection be withdrawn.

REJECTION UNDER 35 U.S.C. § 102/ § 103

The subject matter of the claims was commonly owned at the time the invention was made, therefore 35 U.S.C. 103(c) and the potential 35 U.S.C. 10(e), (f), or (g) prior art under 35 U.S.C. 103(a) is not applicable.

Claims 27-29, 33-36, 40-43, and 47 stand rejected under 35 U.S.C. § 102(e) as being anticipated by or in the alternative under 35 U.S.C. § 103 as obvious over Hoffmann (U.S. Patent No. 6,358,924.

Applicants respectfully disagree that Hoffmann is an anticipation or an obviousness reference. Hoffmann discloses a formulation that comprises surfactants. Applicants' claimed formulation is void of surfactants. There is no suggestion or motivation to remove surfactant in Hoffmann, but rather it is a necessary component of the formulation to provide for oral absorption or long term storage. Applicants request reconsideration and withdrawal of this rejection.

SUMMARY AND CONCLUSION

Applicants respectfully assert that the application is now in condition for allowance. The claims are enabled. The claims are definite and particularly point out and distinctly claim the subject matter being sought. The shelf stable solution formulation is neither anticipated nor obvious in view of the cited references. If, for any reason, the Examiner feels that a telephone conversation would be helpful in expediting the prosecution of this case, the Examiner is urged to call me.

Respectfully submitted,

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